The use of cryopreserved femoral vein grafts for hemodialysis access in patients at high risk for infection: A word of caution

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Background: **Several studies have reported success in the use of venous homografts for arteriovenous access and for arterial bypass in infected fields. On the basis of these reports and in an effort to prevent the loss of vascular access to infection, we performed arteriovenous graft placement with cryopreserved femoral vein in patients at high risk for graft infection. This study reviews the results of our experience.**

Methods: **Of approximately 3100 dialysis access operations performed in a single vascular surgery service between October 1999 and July 2001, 20 patients received arteriovenous access grafts with cryopreserved femoral vein. All patients were judged to be at high risk for infection of the access on the basis of the presence of active infection at the time of graft implantation, the location of the graft in the thigh position, or a history of multiple access infections. The grafts were placed in three locations: thigh (n = 14), upper extremity (n = 3), and chest wall (n = 3).**

Results: **No early operative deaths or graft thromboses were seen. There were three late deaths: two from cardiac disease and one from a graft-related complication. Thirteen major graft related complications (65%) occurred in the 20 patients. There were three generalized graft infections (15%) and eight localized graft infections (40%) at dialysis needle access sites in 11 patients. Six of the graft infections were associated with graft rupture and frank hemorrhage, resulting in one patient death from exsanguination. Two grafts (10%) thrombosed, one of which was salvaged after thrombectomy and revision. These complications occurred between 1 and 14 months after implantation. At a mean follow-up period of 13 months (range, 1 to 17 months), only five of the 20 patients (25%) have a functioning cryopreserved femoral vein arteriovenous graft.**

Conclusion: **The use of cryopreserved vein graft for hemodialysis access in patients at high risk for infection is associated with a high incidence rate of graft infection and rupture, particularly when placed in the thigh position. The routine use of cryopreserved vein graft in the thigh should be avoided. The in situ replacement of infected polytetrafluoroethylene arteriovenous grafts with cryopreserved vein should be considered if alternative sites for new access placement are unavailable. (J Vasc Surg 2002;36:464-8.)**

As the demographics of the patient population on hemodialysis has shifted to older and sicker patients, an associated increase has been seen in the utilization of arteriovenous grafts for hemodialysis access.[1] Accompanying this rise in utilization of arteriovenous grafts has been an increase in the incidence of graft infection, which occurs at a rate of approximately 16% overall and between 18% and 35% in the thigh position.[2-4] Several innovative techniques have been described for treating arteriovenous graft infection while preserving sites for future arteriovenous access placement.[5,6] One method proposed by Matsuura et al[7] is complete graft excision with in situ replacement with cryopreserved femoral vein graft. The authors showed favorable results with the technique in a series of patients with infected arteriovenous grafts primarily in the arm position.[7] Other investigators have reported the successful use of cryopreserved allografts as conduits for vascular reconstruction in infected fields.[8,9] These encouraging results prompted us to use cryopreserved femoral vein grafts in a group of patients undergoing arteriovenous graft placement who were considered at high risk for graft infection. This study reviews our experience with the cryopreserved femoral vein for arteriovenous graft placement in this highly selected patient population.

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PATIENTS AND METHODS

From October 1999 to July 2001, 3100 dialysis access operations were performed by the vascular surgery service at Greenville Memorial Hospital. During this period, 20 patients underwent arteriovenous graft placement with cryopreserved femoral vein. In each case, the decision to use cryopreserved vein was based on a determination by the attending surgeon of increased risk for subsequent graft infection. The factors used to determine this risk were location of the graft in the thigh position (n = 14), the need to place the graft into an infected field (n = 4), and a history of multiple previous arteriovenous graft infections (n = 4).

Two patients had two risk factors for subsequent access infection (thigh position and active infection).

The grafts were placed in the thigh position in 14 cases, in the arm in three cases, and on the chest wall (axilloaxillary loop graft) in three cases. Patient characteristics are shown in the Table. The ABO type of the implanted graft matched that of the patient in all cases. All patients received perioperative antibiotics. Patients who had grafts implanted directly into infected tissue received intravenous antibiotics for at least 2 weeks after surgery.

The cryopreserved femoral vein grafts (CryoLife, Inc, Kennesaw, Ga) were shipped to the operating room on the morning of surgery. The technique of graft preparation outlined by CryoLife, Inc, was strictly followed in all cases. To ensure quality control, a CryoLife representative was present during the graft preparation for the initial patient. All of the thigh and chest wall grafts (n = 17) were constructed in a loop conıguration with two cryopreserved femoral vein segments sewn end to end before implantation. The arm grafts (n = 3) were constructed in a straight conıguration with one cryopreserved vein segment. The lot numbers of the grafts implanted into each patient were different. No graft was accessed for hemodialysis earlier than 6 weeks after graft implantation. Data were obtained from office and hospital charts and our vascular registry. Patients were generally seen in the office after surgery at 2 weeks and at 6 weeks. After a series of graft-associated complications were recognized, a graft surveillance program was instituted that involved dialysis unit education and office follow-up every 3 months.

RESULTS

No 30-day operative deaths occurred in the study. There were three late deaths: two from cardiac disease and one from exsanguination from graft rupture. Major graft-related complications occurred in 13 of 20 cases (65%). Eleven patients (55%) had graft infection develop. The diagnosis of graft infection was based on clinical findings of generalized erythema and tenderness over the graft with associated fever and leukocytosis in three patients, pseudoaneurysm of the graft at a needle access site with associated erythema and tenderness in four patients, and pseudoaneurysm of the graft at a needle access site with skin ulceration and graft rupture in four patients. Culture results were obtained in two patients with generalized graft infection who were found to have perigraft fluid at the time of graft excision. Culture of the fluid was negative in both patients. At the time of graft excision, both patients had systemic signs of sepsis and one patient had a staphylococcal bacteremia. In both cases, the patient's sepsis resolved after graft excision. Culture results of the wounds or vein grafts in the other patients with graft infection were not obtained. All of the graft infections that developed were at sites remote from the surgical incisions, after apparent healing and after initiation of hemodialysis. Six of the grafts with localized infection were excised. Two grafts were salvaged with resection of the involved graft segment and restoration of graft continuity with polytetrafluroethylene graft that was routed through uninfected tissue.

Patient demographics and complication rate

Patient characteristic	*Total number*	*Total complication*
Male gender	8	6
Female gender	12	7
Black	12	10
White	8	3
Diabetes	8	4
Peripheral artery disease	6	3
Coronary artery disease	5	2
Obesity	3	3

Infection occurred in 64% (9/14) of the thigh grafts, 33% (1/3) of the arm grafts, and 33% (1/3) of the chest wall grafts. Cryopreserved femoral vein grafts were used for in situ replacement of infected polytetrafluroethylene arteriovenous grafts in the thigh in two patients, in the arm in one patient, and in the chest wall in one patient. One of these grafts placed in the thigh position subsequently became infected and ruptured. The remaining grafts (3/4, 75%) showed no signs of infection, although the graft in the arm thrombosed at 6 months and was revised. The infections occurred between 1 month and 14 months after graft implantation. At the time of diagnosis of cryopreserved vein graft infection, no patient had a dialysis catheter in place.

Two upper extremity grafts thrombosed at 5 months and 6 months after implantation. Only one of the grafts could be salvaged with thrombectomy and revision. Overall, at a mean follow-up period of 13 months (range, 1 to 17 months), only five patients (25%) have a functioning cryopreserved femoral vein arteriovenous graft.

Graft patency was analyzed with life-table analysis. At 17 months, the primary graft patency rate was 28% and the secondary patency rate was 31%.

DISCUSSION

Recently, Matsuura et al[7] reported results of a series of 44 patients who underwent placement of cryopreserved femoral vein grafts for hemodialysis access. Although most grafts were implanted in infected patients, with many grafts implanted directly into infected tissue, no graft infections occurred.[7] Other investigators have duplicated this success with the use of cryopreserved vein as an arterial bypass conduit implanted in situ into infected fields for vascular reconstruction.[8] The prospect of a graft that is resistant to infection has enormous implications for the patient population on hemodialysis. Infection is responsible for substantial cost and morbidity associated with hemodialysis access.[1,10] Arteriovenous graft infection is even more devastating in the patient who has limited sites for access placement because it can mean loss of that site for future access use. Perhaps those most at risk for graft infection are patients with arteriovenous grafts placed in the thigh position. In a series by Bhandari, Wilkinson, and Sellars,[3] infection occurred in 35% of arteriovenous grafts placed in this position. We recently reported results from our insti-

tution with polytetrafluoroethylene arteriovenous grafts in the thigh. We noted an 18% incidence rate of infection, which is substantially higher than that reported for arm grafts.[4,11]

Benedetto et al[12] reported that the use of cryopreserved vein precludes kidney transplantation because of allosensitization. Also, the cost of cryopreserved vein is five to 10 times that of polytetrafluoroethylene, depending on whether one or two segments of the vein are used. We reasoned that these disadvantages of cryopreserved vein would be outweighed by the advantage of its resistance to infection and that the infections prevented would offset the cost differential between cryopreserved vein and polytetrafluoroethylene. Therefore, in an effort to salvage dialysis access sites despite the presence of infection and to prevent infection in patients considered to be at high risk for graft infection, we chose to use cryopreserved femoral vein grafts for arteriovenous access in a group of 20 selected patients. Unfortunately, we found a high incidence rate of major complications associated with cryopreserved femoral vein arteriovenous grafts. During a 14-month period, a major complication occurred in 65% of grafts. Most alarming was the high incidence rate of graft infection and rupture, which occurred with one associated death. Other investigators' experiences with cryopreserved vein graft for arteriovenous access and arterial reconstruction have suggested that the patency is similar to that achieved with prosthetic grafts.[7,13] Our patency results may not be a true reflection of the patency expected from this graft because many of our grafts were lost early because of infection.

We had strikingly different outcomes with cryopreserved femoral vein grafts for hemoaccess compared with those obtained by Matsuura et al.[7] The percent of patients who were at greatest risk for development of subsequent graft infection, grafts placed directly into infected fields, were similar between the two studies with nine of 44 (20.5%) in Matsuura et al's[7] study and four of 20 (20%) in our series. Matsuura et al's[7] indication for use of cryopreserved vein graft in the remainder of patients in the series was for localized infection, which was bypassed through noninfected fields in 11 of 44 patients (25%), for bacteremia and sepsis in 14 of 44 patients (31.8%), and for multiple graft failures in 10 of 44 patients (22.7%). The indication for usue of cryopreserved femoral vein grafts in the remainder of patients in our series were for multiple graft infections in three of 20 patients (15%) and need for access placement in the thigh position in 14 of 20 patients (60%). These differences in indication for cryopreserved vein graft placement resulted in a significantly greater number of grafts placed in the thigh position in our series. Perhaps differences in skin flora between the upper extremity and the thigh render the thigh graft more susceptible to infection and explain the difference between the results of the two series.

Three patients in our series died during the period of review. Two of the deaths were cardiac related, and one death was from exsanguination from a vein graft rupture. Our previous study noted a 33% mortality rate in the patient population in the thigh position. However, none of these deaths were access related.[4] No studies have specifically addressed the incidence of access-related death.

Our experience is similar to that of Berman et al[14] who reported on a small series of patients who underwent arteriovenous access placement with cryopreserved saphenous vein grafts. In that series, all the grafts (3/3) placed in the thigh position were lost to pseudoaneurysm and infection.[14]

After several graft ruptures occurred in our series, we instituted a surveillance program of regular follow-up to identify graft problems early. This involves inspecting the pseudoaneurysms and the skin integrity over the grafts. The pseudoaneurysms have been readily apparent on physical examination, and we have therefore not used duplex ultrasonography routinely for surveillance.

Our policy is to revise the graft immediately if a patient has erythema and tenderness develop over a pseudoaneurysm or if the skin integrity over the pseudoaneurysm is poor. For most graft revisions, we have used the technique of segmental bypass with polytetrafluoroethylene and partial graft excision as previously described by our group.[5] Revision of cryopreserved vein arteriovenous grafts can be challenging. The vein is torn easily, and therefore extreme care must be taken during dissection.

CONCLUSION

The use of cryopreserved femoral vein graft for arteriovenous access in our experience is associated with an alarmingly high incidence rate of complications, including infection, graft rupture, and death. Extremely close follow-up is warranted in those patients who are currently undergoing dialysis with cryopreserved femoral vein arteriovenous graft. Complications that arise should be treated early and aggressively. This study suggests that the routine use of the cryopreserved femoral vein graft in the thigh position should be avoided until controlled randomized studies establish its safety and efficacy compared with polytetrafluroethylene grafts. The use of cryopreserved femoral vein graft for in situ replacement of infected polytetrafluroethylene arteriovenous grafts should be considered if alternative sites for new arteriovenous access placement are not available.

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DISCUSSION

Dr John Matsuura (Atlanta, Ga). I would like to thank the authors of this presentation for the opportunity to review the manuscript and President Rosenthal and the society for the opportunity to make a few comments.

William Bolton, David Cull, and colleagues present a series of 20 renal failure patients undergoing placement of cryopreserved femoral vein as an AV graft. Unfortunately, the authors encountered a very high 65% graft complication rate in their series. Two of the grafts thrombosed, but the analysis of graft thrombosis should remain separate from the infectious complications and with a 1-year PTFE primary patency rate of 31% to 49%, two graft failures from thrombosis is not unexpected. However, 55% (11 of 20) developed infection according to the author's definition based on clinical findings alone. One of the weaknesses of this manuscript was the complete absence of any positive cultures. Three developed major infections, and eight had puncture site infections with five grafts developing bleeding that led to one death from exsanguination.

Since 1996, there have been over 1400 cryopreserved femoral vein AV grafts placed in the United States. There is a multicenter prospective database currently being maintained that is tracking over 200 implants. I looked up the 32 thigh AV grafts from this series, and the 1-year primary and secondary patency rate is 61% and 88%, respectively. The graft complications seen in the thigh locations included two anastomotic leaks requiring revision and one access site bleed associated with a pseudoaneurysm similar to the author's experience. There was also one major bleeding event, a contained disruption, from recurrent Serratia marcescens infections. This gives a 13% incidence of serious bleeding complications in our prospective database, which is much higher than my previous experience in the upper arm location. From this standpoint, I would agree with the authors of this paper that the thigh position does have a higher graft complication rate. I would emphasize the higher complication rate is related more to location than conduit as exemplified by Dr Spence Taylor's own publication in the American Surgeon in 1996 on thigh access from your institution. I do have a few questions for Dr Bolton.

Based on the three major graft infections seen in this study, do you feel the virulence of the bacteria should play a role in selecting cryopreserved femoral vein implantation?

Second, I have discovered that excessive tension and clamp injury of these allografts leads to a higher incidence of aneurysms. Do you feel some of the aneurysms in your series may be related to technical errors?

And finally, one of the most common PTFE AV graft complications is pseudoaneurysm with bleeding related to excessive recurrent puncture access at the same location in the graft, the so-called "sweet spot." The clinical presentation is often a tender pseudoaneurysm with bleeding related to skin breakdown and ulceration. Were the eight cases of local infection related to improper access of the same location of the graft, or was it a true infection? If it was an infection, what was the organism? None of the cases presented had a positive graft culture result.

Thank you again for a very good presentation. I look forward to your comments.

Dr William D. Bolton. Thank you Dr Matsuura for your comments and questions.

Regarding your first question on the role of bacterial virulence on infection of cryopreserved femoral vein grafts, we can only speculate since the diagnosis of infection in our series was based upon clinical findings rather than culture results. Our disappointing results with cryopreserved femoral vein are quite different from the favorable results you recently reported. One explanation for the difference is that the majority of grafts in our series were placed in the thigh whereas most of the grafts in your series were in the arm. We surmise that a difference in skin flora between the arm and the thigh renders grafts placed in the thigh position more susceptible to infection.

You asked if clamp injury or tension at the anastomosis is a possible explanation for the aneurysms seen in our series. The handling characteristics of cryopreserved femoral vein are markedly different from that of other graft materials. It is obviously imperative then that the graft is handled gently during implantation because it does not have the wall strength of other graft materials. Seventeen of the 20 grafts in our study were comprised of two vein segments in order to allow for a tension-free positioning. To prevent disruption of the anastomosis and injury to the vein, great care was taken in tunneling so that there would be no tension or damage to the graft. We did place a clamp on the graft near the anastomosis after the initial anastomosis had been completed. The pseudoaneurysms, which occurred, were at needle stick sites, not near the anastomosis; therefore, we do not believe these were related to technical errors of graft insertion.

Finally, you asked if these complications were related to excessive recurrent puncture sites at the same location of the graft. The cryopreserved femoral vein is a large graft usually measuring over 10 mm in diameter. The majority of grafts in our series were placed in a loop configuration using two vein segments. This provided a larger graft area such that the dialysis nurse should have little difficulty in finding multiple sites to access these grafts. The fact that the graft complications occurred in eight different dialysis

units in our community also leads us to believe that these were not due to improper sticks.

Thank you.

Dr Charles Kiell (Hickor, NC). I have had experience, a short experience, with using the saphenous vein as a conduit for lower extremity reconstruction when there was no usable alternative and amputation was the only option. My experience somewhat mirrored yours in the fact that I had two cases of rupture, both in multiple redo patients at the proximal end of the graft, and in neither case was the rupture at the site of the anastomosis but was at a small area of necrosis within the vein graft. One occasion led to the patient's death while at home. In both instances, I was able to examine the graft. The second one I was able to see at the time of reexploration, and in both, there was a very small pin hole leak that any other time you would have expected the leak to stop spontaneously and in both cases the graft had virtually not incorporated at all into the adjacent tissues. The reason why I bring it up to convey the experience is to me this said something about the graft behavior of how it incorporates to adjacent living tissue and, because the bleeding occurred from very small areas, how it behaves as a site for normal coagulation and thrombosis to occur that normally one would have expected this to have sealed off spontaneously.

Dr Alan Lumsden (Houston, Tex). Let me put this in perspective. This is not a first-line AV access graft. This is not the graft you use in the easy case. It is a graft that is considered only in situations where the site is infected or you are on your last legs or you have multiple thromboses of a PTFE graft. So you cannot really compare the complication rate with de novo PTFE grafts.

The second issue is that the way that this is approved since it is a tissue, this comes to clinical use in a very different way from PTFE grafts, which go the device route. Cryovein has not been tested through multicenter randomized trials as it probably should be, so it is not surprising to hear some of these complications.

I have used this graft. I have not seen the same complications you have, but no question they get pseudoaneurysms. Technically, they are very difficult to revise because they are very thin, they are very stuck, and it is an extraordinarily difficult procedure to try and revise a pseudoaneurysm.

Having said that, I have never put one in the thigh and the reason for that is because the grafts are short. It is difficult to make a loop graft with a cryopreserved femoral vein graft unless you are going to sew two of them together. That makes it very expensive, and it also puts another anastomosis in there and makes it difficult to tunnel. You have to be careful in tunneling that you do not disrupt the anastomoses, and I wonder if any of the complications were related to the fact that you perhaps were having to sew more than one segment of these together.

Dr Bolton. None of the complications occurred at an anastomosis. When placing a graft, which utilized two vein segments, we positioned the counterincision so that it would be over the vein-vein anastomosis. This was done to ensure that the anastomosis could be inspected after flow was established in the graft. As I mentioned earlier, the graft must be handled gently particularly during tunneling.